

AMENDMENTS TO THE CLAIMS

1-86 (Canceled)

87. (Currently amended) A method for assessing at least one quality parameter or at least one quantity parameter of a particle in a liquid material, said liquid material comprising particles having bound thereto or comprised therein at least one species of analytes in an amount of less than 1×10^6 analyte detectable positions per particle,

comprising:

mixing the liquid material with at least one reagent material, said reagent material at least comprising a first targeting species capable of selectively and directly binding to an analyte position of said species of analytes said species of analytes having an amount of less than 1×10^6 analyte detectable positions and a labelling agent, wherein said labelling agent is a compound capable of emitting, absorbing, attenuating or scattering electromagnetic radiation to result in the generation of a detectable electromagnetic signal, wherein the first targeting species and the labelling agent are directly or indirectly coupled to each other,

arranging a volume of a liquid material comprising at least part of the mixture of the liquid material and the reagent material in a sample compartment having a wall part defining an exposing area, the wall part allowing electromagnetic signals from the sample in the compartment to pass through the wall to the exterior,

exposing, onto an array of active detection elements, a representation of electromagnetic signals originating from said labeling agent having passed through the wall part from the sample in the sample compartment, ~~wherein the representation is subject to a linear enlargement,~~ so that

the ratio ~~of the image~~ of a linear dimension of the image on the array of detection elements to the original linear dimension in the exposing domain is smaller than 20:1,

detecting the representation as intensities by individual active detection elements,

processing the intensities in order to identify representations of electromagnetic signals from the particles as distinct from representations of electromagnetic signals from background, and

obtaining the at least one quality parameter or at least one quantity parameter from the result of the processing; wherein the sample is at a standstill during the exposure of the electromagnetic signals onto the array of active detection elements.

88. (Currently amended) The method according to claim 87, wherein the particle is selected from the group consisting of cells, cell walls, bacteria, plasmodia, virus, prions, or fragments of cell walls, fragments of bacteria, fragments of plasmodia, fragments of virus, fragments of prions, clusters of cells, clusters of bacteria, clusters of plasmodia, clusters of prions, or clusters thereof, and macromolecules and beads.

89. (Previously presented) The method according to claim 88, whereby the particle is a bead, to which analytes are bound.

90. (Currently amended) The method according to claim 87, ~~whereby~~ wherein the analyte is selected from the group consisting of proteins, polypeptides, peptides, lipids, carbohydrates, lipoproteins, carbohydrate-conjugated proteins, membrane constituents, receptors, genes, DNA, RNA, or fragments or clusters thereof fragments of proteins, fragments of

polypeptides, fragments of peptides, fragments of lipids, fragments of carbohydrates, fragments of lipoproteins, fragments of carbohydrate-conjugated proteins, fragments of membrane constituents, fragments of receptors, fragments of genes, fragments of DNA, fragments of RNA, clusters of proteins, clusters of polypeptides, clusters of peptides, clusters of lipids, clusters of carbohydrates, clusters of lipoproteins, clusters of carbohydrate-conjugated proteins, clusters of membrane constituents, clusters of receptors, clusters of genes, clusters of DNA, clusters of RNA, and clusters of fragments.

91. (Currently amended) The method according to claim 88, whereby the analyte is bound to a cell membrane or cell nucleus membrane, ~~such as whereby the analyte is a cell receptor.~~

92. (Previously presented) The method according to claim 88, whereby the analyte is comprised in a cell.

93. (Previously presented) The method according to claim 92, whereby the analyte is comprised inside an organelle.

94. (Previously presented) The method according to claim 92, whereby the analyte is located on the surface of an organelle.

95. (Previously presented) The method according to claim 87, whereby the particles have bound thereto or comprised therein at least one species of analytes in an amount of less than 5×10^5 analyte detectable positions.

96. (Currently amended) The method according to claim 87, whereby the particles have between 500 and 50,000 analyte detectable positions (~~average for population~~).

97. (Currently amended) The method according to claim 87, wherein the particles are cells are selected from the group consisting of mammalian cells, insect cells, reptile cells, fish cells, yeast cells, and fungi cells.

98. (Currently amended) The method according to claim 87, wherein the particles are cells are selected from the group consisting of blood cells, sperm cells, and bone marrow cells.

99. (Previously presented) The method according to claim 87, whereby the liquid material comprises at least two different species of particles.

100. (Previously presented) The method according to claim 99, whereby only one of the species of particles has bound thereto or comprised therein the species of analyte.

101. (Previously presented) The method according to claim 87, comprising binding at least two distinct targeting species to at least two distinct species of analyte and labelling the at least two distinct targeting species with two distinct labelling agents.

102. (Currently amended) The method according to claim 87, ~~whereby~~ wherein one species of analyte is selected from the group consisting of ~~CD~~-(Cluster of Differentiation) markers, such as ~~CD3, CD4, CD8, CD16, CD19, CD22, CD34, CD45, CD61, and CD91,~~ Epithelial Membrane Antigen (EMA), Estrogen receptor α (~~ER~~ α), Cytokeratin Human, Cytokeratin 7, Cytokeratin 20, Ki-67/PI, Phosphatidylserine, BCL2 Oncoprotein, ~~suPAR~~ (soluble urokinase Plasminogen Activator Receptor), urokinase, a hormone bound to a receptor, a cell cycle related protein, a marker of apoptosis, and Green fluorescent protein (GFP).

103. (Currently amended) The method according to claim 87, ~~whereby~~ wherein one species of analyte is selected from the group consisting of a chromosomal DNA sequence, a mitochondrial DNA sequence, a chloroplast DNA sequence, a mRNA sequence, a rRNA sequence, a nucleotide sequence comprising a single nucleotide polymorphism.

104. (Currently amended) The method according to claim 87, ~~whereby~~ wherein one species of analyte is a cell cycle related protein, ~~e.g. cycline (such as cyclin D1), tumor suppresser protein (e.g. p53 protein), Epidermal Growth Factor protein (EGF protein), Transforming Growth Factor beta (TGF beta1), Ki 67 protein.~~

105. (Currently amended) The method according to claim 87, ~~whereby~~ wherein the analyte is a cell cycle related protein receptor ~~such as Epidermal Growth Factor Receptor (EGFR), Cyclin Dependent Kinases (e.g. CDK4).~~

106. (Currently amended) The method according to claim 87, ~~whereby~~ wherein one species of analyte is a marker of apoptosis, ~~e.g. membrane bound phosphatidylserines, phosphatidylserines targeted with Annexin V, BCL2 oncoprotein.~~

107. (Previously presented) The method according to claim 87, whereby the at least one species of analyte is a medical marker of a disease.

108. (Previously presented) The method according to claim 87, whereby the reagent material comprises more than one first targeting species, each of said targeting species being directed to a different analyte.

109. (Previously presented) The method according to claim 87, whereby the targeting species is an antibody directed to the analyte species.

110. (Previously presented) The method according to claim 87, whereby the targeting species is a nucleotide probe complementary to a sequence of an analyte species.

111. (Currently amended) The method according to claim 87, ~~whereby~~ wherein the targeting species is an in situ hybridisation (ISH) probe.

112. (Currently amended) The method according to claim 87, wherein the liquid material is selected from the group consisting of body fluids, ~~such as blood, urine, saliva, bile, sperm, faeces, cerebro spinal fluid, nasal secrete, tears, bone marrow, and milk, milk products,~~

~~waste water, process water, drinking water, food, feed, and mixtures, dilutions, or extracts thereof~~
milk, milk products, waste water, process water, drinking water, food, feed, mixtures of body
fluids, mixtures of milk, mixtures of milk products, mixtures of waste water, mixtures of process
water, mixtures of drinking water, mixtures of food, mixtures of feed, dilutions of body fluids,
dilutions of milk, dilutions of milk products, dilutions of waste water, dilutions of process water,
dilutions of drinking water, dilutions of food, dilutions of feed, extracts of body fluids, extracts
of milk, extracts of milk products, extracts of waste water, extracts of process water, extracts of
drinking water, extracts of food, and extracts of feed.

113. (Currently amended) The method according to claim 87, wherein the ~~labelling agent~~ reagent material is selected from the group consisting of fluorescently labelled antibodies, and antibodies labelled with reactive molecules.

114. (Currently amended) The method according to claim 87, wherein the ~~labelling agent~~ reagent material is selected from the group consisting of fluorescently labelled nucleotide probes, and nucleotide probes labelled with reactive molecules.

115. (Previously presented) The method according to claim 87, wherein the reagent material further comprises lysing agents and tissue fixative agents.

116. (Currently amended) The method according to claim 87, wherein the ~~reagent material further comprises~~ labeling agent is selected from the group consisting of fluorescence

quenching agents, light absorbing agents, and fluorescence amplification agents (~~e.g. fluoresceyl-tyramine, Cy3-tyramine~~).

117. (Previously presented) The method according to claim 87, whereby the labelling agent is selected from agents giving rise to one or several of the following phenomena: attenuation of electromagnetic radiation, photoluminescence when illuminated with electromagnetic radiation, scatter of electromagnetic radiation, raman scatter.

118. (Currently amended) The method according to claim 117, whereby the labelling agent is selected from the group consisting of fluorescein (FITC), phycoerythrin, R-phycoerythrin (RPE or PE), cyanine dyes (~~Cy dyes~~), ~~Cy3, Cy5, Cy5.5~~, allophycocyanines (APC), ~~indotrimethinecyanines, indopentamethinecyanines~~, acridine orange, thiazole orange, DAPI, propidium iodide (PI), ethidium iodide, 7-aminoactinomycin D, and Per CP ~~or chemically coupled combinations thereof~~.

119. (Previously presented) The method according to claim 87, whereby the recording of image comprises the use of a confocal scanner.

120. (Previously presented) The method according to claim 87, whereby the image is recorded using an array of detection devices.

121. (Previously presented) The method according to claim 87, wherein the image is recorded using a CCD, a CMOS, a video camera or a photon counting camera.

122. (Currently amended) The method according to claim 87, whereby the image is recorded ~~without enlargement~~ so that the linear dimension of the image on the array of detection elements is equal to the original linear dimension in the exposing domain.

123. (Currently amended) The method according to claim 87, whereby the enlargement ratio is below 10, ~~more preferably below 5, such as 4, more preferably below 4 such as 2, more preferably below 2, such as 1.~~

124. (Previously presented) The method according to claim 87 whereby the image is recorded in one exposure.

125. (Currently amended) The method according to claim 87 whereby the image is recorded in two, ~~three or more exposures~~ more than one exposure.

126. (Currently amended) The method according to claim 125, wherein the assessment of the number of particles is obtained on the basis of more than one image, ~~preferably two images, more preferably more than two images, more preferably more than four images.~~

127. (Previously presented) The method according to claim 125, where information about the changes in the image in course of time is used in the assessment of the number of particles.

128. (Previously presented) The method according to claim 87, whereby a distinction between at least two spectral properties of a labelling agent is used to obtain the at least one quality parameter or at least one quantity parameter of the particles.

129. (Previously presented) The method according to claim 87, whereby the recording of an image further comprises exposing a first surface of the sample directly with excitation light from a first light means having at least a first light source, by use of focusing means detecting a fluorescence signal from the first surface of the sample onto a first detection means comprising at least a first detector.

130. (New) The method according to claim 102, wherein the Cluster of Differentiation marker is selected from the group consisting of CD3, CD4, CD8, CD16, CD19, CD22, CD34, CD45, CD61, and CD91.

131. (New) The method according to claim 104, wherein the cell cycle related protein is selected from the group consisting of cycline, tumor suppresser protein, Epidermal Growth Factor protein, Transforming Growth Factor beta, and Ki-67 protein.

132. (New) The method according to claim 131, wherein the cycline protein is cyclin D1.

133. (New) The method according to claim 131, wherein the tumor suppresser protein is p53 protein.

134. (New) The method according to claim 105, whereby the cell cycle related protein receptor is an Epidermal Growth Factor Receptor.

135. (New) The method according to claim 105, whereby the cell cycle related protein receptor is a Cyclin Dependent Kinase.

136. (New) The method according to claim 106, wherein the marker of apoptosis is selected from the group consisting of membrane bound phosphatidylserines, phosphatidylserines targeted with Annexin V, and BCL2 oncoprotein.

137. (New) The method according to claim 112, wherein the body fluid is selected from the group consisting of blood, urine, saliva, bile, sperm, faeces, cerebro-spinal fluid, nasal secrete, tears, and bone marrow.

138. (New) The method according to claim 116, wherein the fluorescence amplification agent is fluorescyl-tyramine or Cy3-tyramine.

139. (New) The method according to claim 118, wherein the cyanine dye is selected from the group consisting of Cy3, Cy5, Cy5.5, allophycocyanines, indotrimethinecyanines and indopentamethinecyanines.

140. (New) The method according to claim 87, whereby the ratio of a linear dimension of the image on the array of detection elements to the original linear dimension in the exposing domain is equal to no more than 4.